Attorney Docket No.: T7106(C)
Serial No.: 10/583,230
Filing Date: June 16, 2006
Confirmation No.: 8226

BRIEF FOR APPELLANT

Sir:

This is a revised Brief on appellant's Reinstatement of Appeal from the Examiner's Rejection of all claims following reopening of prosecution in an Office Action mailed June 24, 2010 in the above-identified application.

Appellants request that the previously paid fees for previous Notice of Appeal and Appeal Brief be applied to the current Appeal in accordance with MPEP 1204.01.

The Commissioner is hereby authorized to charge any additional fees, which may be required to our deposit account No. 12-1155, including all required fees under: 37 C.F.R. §1.16; 37 C.F.R. §1.17; 37 C.F.R. §1.18.; 37 C.F.R. §1.136.

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I. REAL PARTY IN INTEREST

Conopco, Inc., d/b/a Unilever, a corporation of New York is the real party in interest.

II. RELATED APPEALS AND INTERFERENCES

There are no other prior or pending appeals or interferences or judicial proceedings known to appellant, the appellant's legal representative, or assignee which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending Appeal.

III. STATUS OF CLAIMS

Claims 1, 4, 5, 13 and 14 stand rejected in a Office Action mailed June 24, 2010.

Claims 7-12 have been withdrawn

No claims have been allowed.

Claims 2, 3 and 6 have been canceled

Claims 1, 4, 5, 13 and 14 are on Appeal.

IV. STATUS OF AMENDMENTS

No claims were amended subsequent to the Office Action mailed June 24, 2010.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The object of the present invention is to provide a fluid distribution system, allowing to feed several fluid phases to any number of parallel microfluidic units from a single or multiple source for each phase, with substantially the same pressure at the inlet port of each of the microfluidic units, and stability of the flow to small pressure fluctuations or small differences between the resistance of each of the microfluidic units (page 7, lines 4-11).

Independent claim 1 is directed to a microfluidic system including first and second fluid supply sources (original claim 1, page 7, lines 5-6). The first and second supply sources supply at least 1000 microfluidic reactors (page 10, lines 22-23) arranged in parallel (page 7, lines 4-11, page 15, line 14 page 16, line 7 and Figures 1 and 2) via an upstream channel or channels (page 15, line 24 and Figure 1). The upstream channel or channels positioned before the microfluidics reactors (page 9, lines 4-5). The reactors each have at least one downstream channel which is positioned after the reactors (page 9, lines 7-8). For all the reactors (original claim 6), the resistance of each of its upstream channels is at least 10 times larger than the resistance of the downstream channel or channels (page 9, lines 22-24).

Claim 4 specifies that the resistance of all the upstream channels recited in claim 1 is at least 100 times larger than the resistance of the downstream channels (page 9, line 22-23).

Claim 5 specifies that the microfluidic reactors recited in claim 1 are all identical (page 11, lines 4-6).

Claim 13 specifies that the microfluidic system according to claim 1, comprises at least the following 3 layers (page 12, line 8):

(i) an inlet/outlet layer comprising inlet channels for first and second fluid supply source and at least one outlet channel (page 12, lines 9-20);

(ii) a connecting layer comprising a plurality of side channels with varying diameter and/or length (page 12, line 22-32); and

(iii) a microfluidic layer, which comprises microfluidic reactors which are connected to the connecting channels via a port and through the connecting channels are in fluid connection with the inlet and outlet channels of the inlet/outlet layer (page 13, lines 1-10).

Claim 14 specifies that the system recited in claim 13 comprises a plurality of connecting layers connecting a plurality of microfluidic layers to a single inlet/outlet layer (page 14, lines 5-7).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Are claims 1, 4, 5, 13 and 14 enabled under 35 USC 112 first paragraph?

Are claims 13 and 14 indefinite under 35 USC 112, second paragraph?

Are claims 1, 4, 5, 13 and 14 unpatentable under 35 USC 103(a) over Anderson et al (US 2003/0053934)?

Are claim 1, 4 and 5 unpatentable under 35 USC 103(a) over Allen et al (WO 01/128670)?

Are claims 1, 4, 5, 13 and 14 unpatentable under 35 USC 103(a) over Gosh et al (US 5,993,750)?

VII. <u>APPELLANT'S ARGUMENTS</u>

Are claims 1, 4, 5, 13 and 14 enabled under 35 USC 112 first paragraph?

<u>Claim 1</u>

The Examiner asserted that the specification does not provide enablement for *1,000 microfluidic reactors* recited in claim 1. According to the Examiner, the specification does not enable any person skilled in the art to which it pertains to make the invention commensurate in scope with the claims. The Examiner further asserted that the specification is not enabling because it is not clearly stated how 1,000 reactors and channels are being connected. Appellants respectfully traverse this rejection.

Appellants first disclose that their invention is specifically directed to *a fluid distribution system, allowing to feed several fluid phases to any number of parallel microfluidic units from a single or multiple source for each phase* (page 7, line 4-11).

Appellants disclose on page 10, lines 19-23 that *when used for numbering-up the number of microreactors will generally be from 1000 to 100000 and the number of feeding channels is adapted thereto. For example it could be at least 1000 or even at least 50000.* The term "numbering-up" refers to the use of many parallel devices (page 1, lines 29-30). Thus, one expressly taught aspect of the invention is a network including a large number of micro-reactors. The next question to consider is whether appellants adequately teach *how* such an apparatus can be constructed.

Appellants teach on page 14, line 9 to page 16, line 7 in combination with Figures 1 and 2, two alternative embodiments of a microfluids network that can be scaled up to *any number of reactors*. Specifically, appellants, generalize the essential elements required for any number of reactors on page 15, line 14 to page 16, line 8 which in pertinent part states:

The simple microfluidic network presented in Figure 1/2 can be generalized in the following way. A more complex microfluidic network involving the parallel action of at least 2 reactors receiving at least 2 different fluids from at least 2 external sources, with exactly one source per fluid, will require the following elements:

- *(i)* *inlets and outlets for the fluids*
- *(ii)* *"splitting node" splitting the fluids coming from the inlets to the various micro-processing elements.*
- *(iii)* *upstream channels, located between the split and the points where the various fluids meet. These upstream channels are optionally used in the processing, for example for cooling, heating, or otherwise processing the inlet fluids before they join.*
- *(iv)* *joining nodes, where the fluids from the at least two sources meet and start to interact; these joining nodes may be the reactors.*

(v) *Downstream channels, located after the joining node, respectively after the reactors, and leading to either the outlets or any collecting channel or gutter which collects the output from the various processing elements. The downstream channels are optionally used to further process the at least two fluids together.*

Appellants' respectfully submit that the above teachings and other teaching found in the specification would have provided adequate guidance to a person of ordinary skill in the relevant art to which the invention pertains (e.g., graduate physical chemist, chemical engineer or physicist with several years of experience in fluids mixing) to design and construct a microfluids system having 1,000 micro-reactors or more.

For example, the artisan could have designed the network simply by starting with the apparatus diagrammed in Figure 1 and the generalized prescription discussed above and given on page 15, line 14 to page 16, line 8, and progressively add splitting nodes to the α and β paths (α1, α2, α3,.....and β1, β2, β3....) each ending at joining nodes which could simply be the inlet of each mico-reactor (1, 2, 3, ...). The skilled person again following the generized plan, would add downstream channel or channels for outflow from each micro-reactor (γ1, γ2, γ3,....pathways) which leads to either the outlets or any collecting channel or gutter which collects the output from the various processing elements.

The artisan could have chosen for example, to fabricate the device from individual tubes, splitting nodes (e.g. "T" connectors) and micro-reactors (e.g. opposing nozzles) as in Figure 1. However, the specification teaches that a three-layer construction is preferable (page 12, line 8). In this embodiment, appellants suggest (page 13, lines 13-16) that a large number of channels or micro-reactors could be etched on an individual surface much like an integrated circuit board. Appellants submit that such fabrication methods are known in the art, e.g., laser ablation (page 13, lines 15-16).

For example, appellants teach on page 12 , line 8 to page 14, line 7 a microfluidic system that *comprises at least 3 layers*: an inlet/outlet layer comprising inlet channels for the first and second fluid supply sources and at least one outlet channel; a connecting layer comprising a plurality of side channels with varying diameter and/or length; and a microfluidic layer, which comprises the microfluidic reactors which are connected to the connecting channels via a port and through the connecting channels are in fluid connection with the inlet and outlet channels of the inlet/outlet layer.

The materials and method of fabrication used to construct the layers are also disclosed. Appellants, for example point out that in a preferred embodiment of the invention, the microfluidic layers need only be etched on their surface, which may be made using a variety of *easily accessible microfabrication techniques*, including, but not limited to, wet and dry etching, molding and laser ablation.

Based at least on the above arguments appellants respectfully submit that claims 1, 4, 5, 13 and 14 are fully enabled by the specification.

Are claims 13 and 14 indefinite under 35 USC 112, second paragraph?

<u>Claim 13 and 14</u>

The Examiner further asserted that in regard to claim 13 it is unclear "how each layer is connected and functions together, in example, are the layers connected horizontally or stacked on each other. It is unclear how the inlet/outlet channels are connected to the reactors".

Appellants respectfully direct the Boards attention to page 12, lines 8 to page 13, line 21 of which the most pertinent sections are:

> Preferably the microfluidic system comprises at least 3 layers. The first layer comprises at least two main inlet channels for fluid supply, and at least 1 outlet channel. This layer is also referred to as inlet/outlet layer. *The inlet and outlet channels are preferably arranged parallel* ......
>
> The connecting layer is preferably positioned *between* the inlet/outlet layer and the microfluidic layer. The connecting layer comprises a plurality of side channels with varying diameter and/or length. This difference in diameter/length enables control over the pressure and flow rate conditions experienced by the microfluidic elements connected to the channels of the connecting layer. ...
>
> The third layer is the microfluidic layer, which comprises a plurality of microfluidic reactors. *These reactors are connected to the connecting channels via a port* and through the connecting channels they are in fluid connection with the main channels that provide the feeding material. ......
>
> Preferably the at least three layers are connected to each other using conventional techniques such as clamping, bolting, bonding e.g. by high temperature treatment, depending on the material that is used.

Appellants submit that a graduate physical chemist or chemical engineer with several years experience in fluids mixing, i.e., a person of ordinary skill in the art, armed with the above description of a three-layer system and the generalized scale-up description discussed above (with Figures 1 and 2) could have constructed either *a horizontial or stacked apparatus*. *Both* types of apparatus would be within the scope of the invention and the choice would depend on space requirements and other factors. Furthermore, a technologist with this background and level of experience would have surely understood how to connect inlet/outlet channels to the reactors, i.e., use appropriate couplings such as switch-locks as suggested by appellants (page 13, 26-27).

Appellants further submit, that if time and expense warranted it, the artisan would have recognized that a modular type of 3-layer "cassette" system where the input/output layer, connecting layer and micro-reactor layers are stacked together and fastened would have been advantageous from the standpoint of compact size and minimization to tubing. Furthermore, these types of modular systems are well known in the microfluids art (e.g., stacked multi-well plates).

Based on the above discussion, appellants therefore submit that the metes and bounds of claim 13 are clear and definite.

Claim 14 specifies that the system comprises a plurality of connecting layers connecting a plurality of microfluidic layers to a single inlet/outlet layer. Appellants have described above, in connection with claim 13 how an apparatus can be constructed that connects a plurality of connecting layers to a plurality of microfluidic layers. Claim 14 specifies that these connecting and microfluid layers are connected to a single inlet/outlet layer.

Appellants disclose on page 12, lines 1-12 that

"The first layer comprises at least two main inlet channels for fluid supply, and at least 1 outlet channel. This layer is also referred to as inlet/outlet layer. The inlet and outlet channels are preferably arranged parallel. Their internal diameter is preferably from 0.1 micrometer to 500 micrometer more preferred from 10 to 250 micrometer.

The channels may be fabricated using a variety of techniques, such as conventional moulding, drilling and the like. The base material for the first layer is preferably selected from the group comprising stainless steel, glass or polymer such as plastic, or a combination thereof."

Appellants' submit that a person of ordinary skill in the art, having this description before him, and available knowledge of multi-well micro-reaction systems such as are used routinely in for example ELISA analysis would have readily understood how to make appellants system employing a single inlet-outlet layer.

Are claims 1, 4, 5, 13 and 14 unpatentable under 35 USC 103(a) over Anderson et al (US 2003/0053934)?

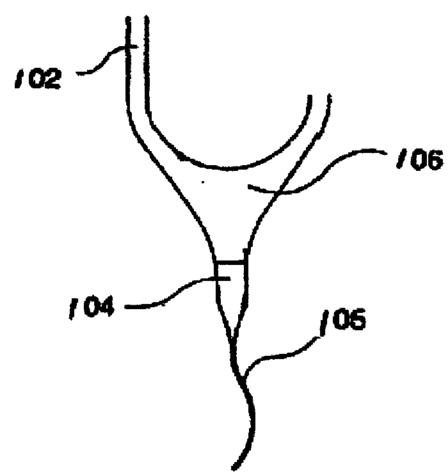
<u>Statement of Facts</u>

Anderson is directed to microfluidic device which comprises two or more microchannel structures (set 1), each of which comprises a structural unit which comprises (i) one or more inlet microconduits, and (ii) an outlet microconduit downstream said one or more inlet microconduits, and (iii) a flow path for a liquid passing through either of said inlet microconduits and said outlet microconduit. *The device is characterized in that each outlet*

microconduit in said two or more microchannel structures is a *<u>restriction microconduit</u>* (Abtract – emphasis added).

Anderson specifically teaches at page 3, [0030] that "the structural unit and also the microfluidic device are characterized in that there are means for creating a significant pressure drop in the *outlet microconduits* (105,205,305) (*restriction microconduit*) and possibly also in the microcavities (104,204,304), if present. The flow through the individual microchannel structures, in particular the inventive structural units (as shown in FIG. 1), on a microfluidic device is preferably under common flow control".

FIG 1



105 is an "outlet microconduit (restriction microconduit)" – [0030] and [0042]

104 is a "microcavity" – [0041]

102 is an inlet microconduit - [0041]

In contrast, appellants' microfluids system requires that *for all the reactors, the resistance of each of its upstream channels is at least 10 times larger (100 time larger* in the case of claim 4*) than the resistance of the downstream channel or channels.*

Claims 1, 5, 13 and 14

To qualify as a 103(a) reference "The prior art reference, or combination of references, must teach or suggest all of the claim limitations (MPEP §2143). In addition to providing at least a suggestion of all the claim limitations, both the suggestion and the reasonable expectation of success must be found in the prior art references, not in Appellant's disclosure" (See In re Vaeck, 20 U.S.PQ.2d 1438, 947 F.2d 448 (Fed Cir. 1991)

Appellants respectfully submit that Anderson does not teach or suggest a microfluidics system in which *for all the reactors, the resistance of each of its upstream channels is at least 10 times larger (100 time larger in the case of claim 4) than the resistance of the downstream channel or channels.*

Appellants submit that this limitation is diametrically opposed to the teaching of Anderson. Anderson specifically requires a device characterized in that each outlet microconduit **105** (which correspond to appellants downstream channels defined as channels that are positioned after the two fluid streams meet - page 9, lines 7-8) must be a *restriction microconduit* and thus must have a higher resistance than the inlet microconduit **102** (which corresponds to appellants' upstream channels defined as channels positioned before the fluids meet – page 9, lines 1-4). This is also clear from Anderson FIG 1 in view of the analysis of resistance taught by Appellants' on page 2, lines 2-23, especially lines 14-20 which is summarized below.

In the simplest case of channels of circular cross section, the resistance R is given by:

$$R=(8*m*L)/(\pi*d^4),$$

where L is the length of the channel and d its diameter.

Thus, for each reactor, the condition that $R_u \geqq 10 R_d$ requires that

$$L_u/(d_u^4) \geqq 10L_d/(d_d^4) \text{ or } L_u(d_d^4) \geqq 10L_d(d_u^4)$$

where R_u, L_u, and d_u are the resistance, length and diameter of the upstream channel and R_d, L_d and d_d are the resistance, length and diameter of the downstream channel.

Thus, appellants teach that the ratio of resistances of the fluid in channels upstream and downstream to each micro-reactor can be controlled to achieve the resistance limitation recited in claims 1 (or 4) at least by using circular channels and by choosing diameters and lengths for each upstream and downstream channel pair to satisfy the above equation. Since quantitative relationships for non-circular channels are also known from fluid dynamics, similar relationships for channels of non-circular cross section can also be derived.

In contrast, the system taught by Anderson can never satisfy the inequality, $L_u(d_d^4) \geqq 10L_d(d_u^4)$ because the diameter of the upstream channel (**102**) is always much greater than the diameter of the downstream channel (**105**). Consequently, appellants respectfully submit that Anderson in fact <u>teaches away</u> from the limitation recited in appellants' claims because Anderson specifically requires a device characterized in that each outlet microconduit **105** (downstream channel) must be a *restriction microconduit* and thus must

have a higher resistance than the inlet microconduit **102** (upstream channel) as is evident from Fig. 1 above.

Absent disclosure of a microfluidics system wherein for all the reactors, the resistance of each of its upstream channels *is at least 10 times larger* than the resistance of the downstream channel or channels either explicitly or implicitly and the teaching away from this limitation, Anderson can not present a *prima facie* case of obviousness over claims 1, 4, 5, 13 and 14 at least because these claims incorporate this limitation.

Claim 4

Claim 4 is even further removed from Anderson because it recites an even bigger difference in resistance (100 fold) between upstream and downstream channels, a limitation taught away from by Anderson.

Are claim 1, 4 and 5 unpatentable under 35 USC 103(a) over Allen et al (WO 01/128670 – hereinafter "Allen")?

Statement of Facts

Allen is directed to "a fluidic mixer that mixes two fluids without using mechanical stirrers. The two fluids are fed into an interaction cavity under predeterminable conditions that ensure the fluid flows oscillate and feed in an alternating manner two exit channels. The fluids in the exit channels form interleaved layers having widths related to the frequency of oscillation." (Abstract – emphasis added)

Thus, Allen is concerned with an individual reactor which is designed to oscillate its output stream between two exit channels.

Allen is silent concerning the problem addressed by appellants, namely a microfluidics distribution system that feeds a large number of reactors, e.g., greater than 1000, that is stable to small pressure fluctuations in the distribution channels and shows reduced occurrence of multiphase shunts (page 8, lines 19-21).

Appellants found that "when the resistance of the upstream channel or channels is 10 times higher, preferably 100 times higher than the resistance of the down stream channel or channels, the influence of small variations in flow rate in either of these channels is limited and hence a more robust system is provided" (page 9, lines 15-20 and 22-4).

Appellants' Arguments

Claims 1 and 5

To qualify as a 103(a) reference "The prior art reference, or combination of references, must teach or suggest all of the claim limitations (MPEP §2143). In addition to providing at least a suggestion of all the claim limitations, both the suggestion and the reasonable expectation of success must be found in the prior art references, not in Appellant's disclosure" (See In re Vaeck, 20 U.S.PQ.2d 1438, 947 F.2d 448 (Fed Cir. 1991)

Appellants respectfully submit that Allen et al does not present a case of *prima facie* obviousness under § 103(a) at least because Allen neither teaches nor suggests the first and second supply sources supplying *at least 1000 microfluidic reactors arranged in parallel* via an upstream channel or channels, said upstream channel or channels positioned before the microfluidics reactors, the reactors each having at least one downstream channel which is positioned after the reactors, wherein for *all the reactors*, *the resistance of each of its upstream channels is at least 10 (or 100* in the case of claim 4*) times larger than the resistance of the downstream channel or channels.*

Allen is silent about the influence of the relative resistance of liquids in upstream and downstream channels on flow stability in a multi-reactor, fluid distribution system when connecting a large number of parallel reactors, let alone that the resistance of *each of its upstream channels being at least 10 (or 100) times* larger than the resistance of the downstream channel or channels in order to minimize fluctuations and eliminate shunts.

Because it is well known in the art of fluid dynamics that varying cross-sectional dimensions results in varying flow rates, the Examiner asserted that it would have been obvious to one having ordinary skill in the art at the time of the invention to have modified the channel dimensions to increase the resistance of upstream channels at least 10 or 100 times (claim 4) larger than the resistance of the downstream channels *to change the flow rate to modify mixing and reaction rate of fluids.*

However, if the motivation to modify channel dimensions were solely based on the desire *to modify mixing and reaction rate of fluids*, appellants submit that the artisan could equally well have reduced the dimensions of some of the downstream channel (as was done in fact by Anderson discussed above) to achieve an equal or higher resistance in the down stream channels than some or all of the upstream channels. This arrangement is in fact

taught by Allen in **Fig 6** where downstream from mixer **612** is channel **616** which serves as *the upstream channel* relative to channels **624**. Since the diameter of channel **624** is smaller than channel **616**, Allen teaches an example where the resistance of a downstream channel (**624**) is much higher than the resistance of its corresponding upstream channel (**616**).

Allen does not deal with a system that involves distribution to a large number of micro-reactors, is silent regarding the problem of instability in such a multi-reactor system, and offers no guidance how this problem should be solved. Allen specifically does not teach or suggest that the relative resistance of flow in upstream Vs downstream channels is a *results-effective variable* as it relates to fluid distribution in a multi-reactor system of the type to which appellants' claims are directed.

MPEP 2144.05B requires that a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

The scale up to a large number of microreactors (i.e., at least 1000) can not be considered as routine on the basis of Allen because Allen does not teach or suggest a key results-effective variable that could be used to ensure that flow to such a large number of reactors is uniform and stable.

Appellants respectfully submit that the Examiner's arguments are based on hindsight using the knowledge gained from appellants' disclosure as a blueprint to reconstruct their claimed invention from the disclosure of Allen. This approach contravenes the statutory mandate of §103 which requires judging obviousness at the point in time when the invention was made. *Grain Processing v. American Maize-Prods. Co.*, 840 F.2d 902, 907 (Fed. Cir. 1988).

Claim 4

Claim 4 is even further removed from Allen because it recites an even bigger difference in resistance (100 fold) between upstream and downstream channels, a limitation not contemplated by Allen.

Are claims 1, 4, 5, 13 and 14 unpatentable under 35 USC 103(a) over Gosh et al (US 5,993,750)?

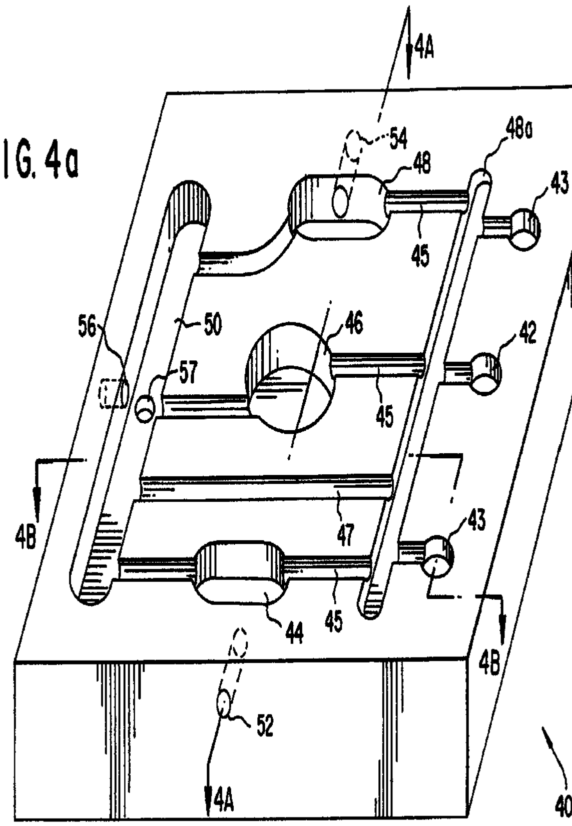
Statement of Facts

Gosh discloses an integrated micro-ceramic chemical plant having a unitary ceramic body formed from multiple ceramic layers in the green state which are sintered together including the unitary ceramic body defining a mixing chamber and passage means for providing communication with the mixing chamber so that two or more fluids may be delivered to such mixing chamber for mixing or reacting chemicals in the fluids; and the unitary ceramic body including means for delivering the mixed chemicals to exit from the unitary ceramic body. (abstract)

Gosh is silent regarding the flow resistance of channels or any relationship between fluid distribution to a large collection of micro-reactors and the flow resistance of upstream vs. downstream channels.

Gosh teaches in Fig 4a the reaction chamber shown below

FIG. 4a



It is clear from the schematic shown in FIG 4a that Gosh teaches reaction chambers **44**, **46** and **48** which communicate with inlet (or upstream) channels and outlet (or downstream) channels that have the same diameters. Thus, in view of the above discussion on flow resistance, these channels have the same resistance in contrast to appellants' invention.

Appellants' argument

Claims 1, 5, 13 and 14

To qualify as a 103(a) reference "The prior art reference, or combination of references, must teach or suggest all of the claim limitations (MPEP §2143). In addition to providing at least a suggestion of all the claim limitations, both the suggestion and the reasonable expectation of success must be found in the prior art references, not in Appellant's disclosure" (See In re Vaeck, 20 U.S.PQ.2d 1438, 947 F.2d 448 (Fed Cir. 1991).

The Examiner admitted on page 11 of the latest Office action mailed June 24, 2010 that Gosh does not teach a system that includes at least 1000 reactors. The Examiner dismissed this limitation as being obvious without further elaboration of any reason why it would have been obvious.

The Examiner further admitted that Gosh also fails to teach flow resistance. The examiner asserted on page 11 of the June 24 Office Action that:

"Although the reference does not explicitly disclose regarding flow resistance, said limitations are directed to processing of the microfluidic device where the limitation relies on fluid dynamics variable as well as reactor design variables which must take into account for changes in the fluid resistance. The variables, such as mass density, velocity, velocity vectors, energy needed to drive the fluid, volume, pressure, temperature, viscosity, as well as design of the reactor such as size of the reactor, pipe sizes, types, etc. Consequently, said limitations are given little patentable weight. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the channel dimensions to increase the resistance of upstream channels at least 10, 100 times

larger than the resistance of the downstream channels to change the flow rate to modify mixing and reaction rate of fluids."

One of the stated objectives of the present invention is "to provide a fluid distribution system, allowing to feed several fluid phases to any number of parallel microfluidic units from a single or multiple source for each phase, with substantially the same pressure at the inlet port of each of the microfluidic units, and stability of the flow to small pressure fluctuations or small differences between the resistance of each of the microfluidic units (page 7, lines 4-11).

Appellants surprisingly found that the relative resistance of upstream and downstream channels influences the robustness of a microfluidic system (page 7, lines 13-15) that includes a large number of parallel micro-reactors.

Thus, appellants' discovered that by insuring that the resistance of the upstream channels be at least 10, preferably 100, times larger than the resistance of the downstream channels they could prevent flow instability and in particular, multiphase shunts (page 8, line 20-21). Thus, the reason behind the resistance limitation recited in appellants' claims has really nothing to do with modifying mixing and reaction rate of fluids as asserted by the Examiner but only arises when large number of reactors are connected in parallel – a problem which is not even considered by Gosh.

Appellants' submit that in constructing an argument of obviousness, the Examiner is obliged to present a *rational* reason why a person of ordinary skill in the art would have been motivated to modify Gosh so as to derive appellants' invention.

Appellants again submit that it is only through hindsight, using appellants invention as a blueprint could it be considered as having been obvious to introduce multiple mixing layers when Gosh teaches a single layer, and to introduce upstream and downstream channels which have vastly different resistances when Gosh specifically teaches identical resistance. Gosh is silent about the problem of flow instability in feeding large numbers of reactors from single or multiple sources and thus did not recognize the relative resistance of upstream and downstream channels as a results-effective variable.

In summary, Gosh is directed at a different problem from appellants' invention. Absent a teaching or suggestion of the limitations on number of reactors and flow resistances, Gosh does not present a *prima facie* case of obviousness over claims 1, 4, 5, 13 and 14.

Claim 4

Claim 4 is even further removed from Gosh because it recites an even bigger difference in resistance (100 fold) between upstream and downstream channels, a limitation not contemplated by Gosh and in fact, taught away from (**FIG 4a** and above discussion).

In view of the forgoing arguments, appellants respectfully submit that the claims at issue are fully enabled, clear and definite and are not obvious over the references cited by

the Examiner. Appellants respectfully request the Board of Appeals and Interferences to reverse the rejection and have the Examiner issue the claims.

Respectfully submitted,

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MPA/sm
201-894-2412 or 845-708-0188

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VIII. CLAIMS APPENDIX

Claim 1. A microfluidic system comprising first and second fluid supply sources, the first and second supply sources supplying at least 1000 microfluidic reactors arranged in parallel via an upstream channel or channels, said upstream channel or channels positioned before the microfluidics reactors, the reactors each having at least one downstream channel which is positioned after the reactors, wherein for all the reactors, the resistance of each of its upstream channels is at least 10 times larger than the resistance of the downstream channel or channels.

Claim 4. A microfluidic system according to claim 1, wherein the resistance of all the upstream channels is at least 100 times larger than the resistance of the downstream channels.

Claim 5. A microfluidic system according to claim 1, wherein the microfluidic reactors are all identical.

Claim 13. A microfluidic system according to claim 1, wherein the microfluidic system comprises at least the following 3 layers:

(i) an inlet/outlet layer comprising inlet channels for first and second fluid supply source and at least one outlet channel;

(ii) a connecting layer comprising a plurality of side channels with varying diameter and/or length; and

(iii) a microfluidic layer, which comprises microfluidic reactors which are connected to the connecting channels via a port and through the connecting channels are in fluid connection with the inlet and outlet channels of the inlet/outlet layer.

Claim 14. A microfluidic system according to claim 13 wherein the system comprises a plurality of connecting layers connecting a plurality of microfluidic layers to a single inlet/outlet layer.

IX. EVIDENCE APPENDIX

None

X. RELATED PROCEEDINGS APPENDIX

None.